

REMARKS

The specification has been amended to correct the reference to prior applications and use of trademarks. The specification has been further amended to correct the description of the nucleotides corresponding to the coding region of human IL-22 from nucleotides 65 to 601, to nucleotides 71 to 607, of SEQ ID NO:1. SEQ ID NO:1 from priority application USSN 09/561,811 is shorter in length by 6 nucleotides at its 5' end compared to SEQ ID NO:1 as disclosed in the instant application. The coding sequence and corresponding amino acid sequences disclosed in both filings are identical. Thus, the specification has been amended to have the description correspond to the longer sequence introduced in the instant application.

Claims 14, 34-38, 40 and 42 have been amended, and claims 46-62 have been added. Claims 1-9, 11, 15 and 21-33 had been previously cancelled as being directed to the non-elected invention. Upon entry of this amendment, claims 10, 12-14, 16-20, and 34-62 will be pending. No new matter has been added.

Claim 14 has been amended to depend from claim 12. Claims 34-38, 40 and 42 have been amended to depend solely from claim 12, thus eliminating multiple dependent claims. New claims 46-53 have been added to depend from claim 17, which had been previously presented as multiple dependent claims 34-38, 40 and 42. New dependent claim 54 is directed to the treatment of psoriatic arthritis. Support for this claim can be found, e.g., at page 1, lines 20-24 of the specification.

New claims 55-62 have been added. Support for these newly added claims can be found, e.g., on page 10, lines 18-42; page 11, lines 1-13; page 15, lines 1-19; page 23, lines 9-33; page 24, lines 1-13; page 26, lines 6-10; page 33, lines 26-31; page 36, lines 3-33; page 37, lines 1-13; page 45, lines 10-13; original claims 1-6, and in Examples 5-10, of the specification.

Objections to the specification and priority

On page 2 of the outstanding Office Action, the Examiner objected to the reference to USSN 09/561,811 in the priority claim. In response, Applicants have amended the specification to make proper reference to USSN 09/561,811 as suggested by the Examiner.

Applicants have further amended the specification to make proper reference to the trademarks mentioned throughout the specification as indicated by the Examiner.

Rejection of claims 10, 12-14, 16-20, and 34-45 under 35 U.S.C. 103(a)

Claims 10, 12-14, 16-20, and 34-45 were rejected under 35 U.S.C. 103(a) as being obvious over Dumoutier *et al.* (2000, PNAS 97(18): 10144-10149) and U.S. Patent 6,551,799 in view of Llorente *et al.* (2000, *Arthritis & Rheumatism* 43(8): 1790-1800). The apparent basis of the Office's position is that Applicants are only entitled to the priority date of U.S. Application 09/561,811, and thus the claimed subject matter has a priority date of February 23, 2001, which is after the publication/filing dates of the cited references.

Applicants respectfully traverse this rejection and submit that the claimed methods are enabled as early as the filing date of USSN 60/131,473, filed April 28, 1999 (the provisional application from which USSN 09/561,811, filed on April 28, 2000, claims priority to). However, for simplicity, the arguments set forth below will focus primarily on the enabling disclosure in USSN 09/561,811 as of April 28, 2000 since that date pre-dates the publication of the references cited in the instant rejection.

USSN 09/561,811 discloses human IL-22 (referred to in that application as hGIL-19/AE289) amino acid and nucleotide sequence. This application also discloses its characterization as a pro-inflammatory cytokine based on homology to IL-10, and activity *in vitro* and *in vivo* (see e.g., specification starting on page 18, lines 5-12, and lines 31-32, until page 19, lines 1-2; Examples on pages 46-49; and SEQ ID NO:1 and 2, and Figure 1 of USSN 09/561,811). For example, on page 47 of USSN 09/561,811, Applicants show that human IL-22 has cytokine-like activity by inducing the phosphorylation of STAT-3 upon exposure of an IL-22- responsive cell type (MES-13 cells) to IL-22. On page 49 of USSN 09/561,811, Applicants showed, for the first time, the effects of IL-22 *in vivo* in mice, including the induction of an acute phase response upon *in vivo* administration of IL-22, where the specification provides that:

In addition, there were a number of hematological effects that were apparent on day 7, including decreased red blood cell count, hemoglobin, and hematocrit. These effects, taken together, indicated anemia in the animals. Furthermore, there was an increase in platelets as well as an increase in the white blood cell count due to an increase of neutrophils. In light of these observations there was no evidence of a regenerative response, which indicated that the effects can be at the level of the bone marrow.

Furthermore, there was a slight decrease in Albumin levels at day 7 and day 14. (page 49, lines 13-20 of of USSN 09/561,811)

These changes in response to *in vivo* administration of IL-22 described above were known at the time to be indicative of an acute phase, pro-inflammatory response (see Gabay, C. and Klushner, I. (1999) *New England Journal of Medicine* 340 (6):448-454, Tables 1 and 3 for a summary of the changes during an acute phase response¹).

Moreover, USSN 09/561,811 discloses antibodies against human IL-22, as well as methods of making and using such antibodies to treat autoimmune disorders, e.g., rheumatoid arthritis (see e.g., starting at page 42, line 29, through page 44, line 2, of USSN 09/561,811 for an enabling disclosure of anti-IL22 antibodies and methods of generating the same; see also page 19, lines 26-29, page 23, lines 30-33, for a disclosure of autoimmune disorders to be treated). The description of autoimmune disorders in the specification (discussed above) is followed by several pages describing different mechanisms by which immune suppression or down-regulation can be effected, and concludes by stating that:

The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythematosus in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., *Fundamental Immunology*, Raven Press, New York, 1989, pp. 840-856²). (specification at page 25, lines 27-33 of USSN 09/561,811)

Thus, well-characterized and reasonably predictive animal models for many of the autoimmune disorders encompassed by the claims were disclosed in the specification and were available to the skilled artisan at the time USSN 09/561,811 was filed. In view of the disclosure showing how to make and use the aforesaid anti-IL22 antibodies, as well as their testing on well-characterized animal models available at the time, the skilled artisan would have been able to evaluate the activity of such antibodies in treating several of these disorders without undue experimentation at the time USSN 09/561,811 was filed. Applicants also submit that a disclosure on how to make and use anti-IL22 antibodies in treating autoimmune disorders similar to the one described above for USSN 09/561,811 can also be found in USSN 60/131,473, filed on April 28, 1999 (see e.g., page 22, lines 3-12; page 23, lines 30-34; page 24, lines 1-4 of USSN 60/131,473). Therefore, an enabling disclosure for the claimed subject matter is provided as early as April 28, 1999, which pre-dates the publication or filing date of all of the references cited by the Examiner.

¹ Submitted herewith as Exhibit 1.

² Submitted herewith as Exhibit 2.

Therefore, because USSN 09/561,811 (and its parent application USSN 60/131,473) provide an enabling disclosure, and the filing date of USSN 09/561,811 (i.e., April 28, 2000) pre-dates the publications by Dumoutier *et al.* and Llorente *et al.* (both of which were published in August of 2000), Applicants respectfully submit that these references are not prior art against the instant application. Moreover, US 6,551,799 is directed to IL-22 and uses of IL-22 antagonists to treat pancreatitis. Applicants submit that USSN 60/131,473 (from which USSN 09/561,811 claims priority) provides an enabling disclosure of the claimed subject matter as of April 1999. Such disclosure pre-dates the filing of the priority date claimed in US 6,551,799 (which has an earliest filing date of December 7, 1999). Thus, none of the references cited by the Office is prior art against the instant application.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

Applicants submit that the present application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at (617) 665-6073.

A petition for Three-Month Extension of Time is submitted herewith. Please charge the required extension fee to Deposit Account No. 07-1060 (Reference No. GI 5358 CIP). The Commissioner is hereby authorized to charge any additional fees required in connection with the above-referenced application, or to credit any overpayment of same, to Deposit Account No. 07-1060 (Reference No. GI 5358 CIP).



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